Bandolier 79

What do we think?
What do we know?
What can we prove?

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Electronic Bandolier

Regular visitors to the ***Bandolier*** Internet will have seen a number of changes over the last few months. There will be more in coming months, as Internet ***Bandolier*** becomes much, much more than an electronic form of the paper edition. To list what is there right now:

- Every issue of ***Bandolier*** and ***ImpAct*** in portable document format, downloadable to your computer and printable on your printer, as well as viewable on screen.
- Thirty one specialist subsections, where we have brought together topics featured in ***Bandolier*** and ***ImpAct*** and subdivided them for easy access.
- A new whizzo search engine that accesses the whole site to find a particular topic, wherever it is.
- A Spanish language edition of ***Bandolier*** (called ***Bandolera***) from issue 65, and with a growing library of translated stories from past issues.

Specialist subsections	Number of articles
Asthma, allergy and chest	19
Bones and joints	24
Cancer	17
Cardiac	23
Complementary therapy	51 and growing
Dental	5
Diagnostics	49
Drug abuse	7
EBM stories	58
ENT	8
Family health	16
Gastrointestinal	29
Genetics	9
Healthy living	25 and growing
HIV Aids	3
Management	130 and growing
Men's health	28
Mental health	10
Migraine	16 and growing
Neurological	13
NNTs	10
Older people	48
Oxford Pain Internet Site	132 and growing
Perioperative issues	31
Pharmacy	10
Screening	13
Sexually transmitted disease	9
Trial Methods etc	19
Urinary	14
Women's Health	50
Book reviews	35

More services

The intention is to keep the Internet site growing much faster than we can deliver information through the paper version. A list of specialist subsites is shown in the Table. For several of these we have obtained sponsorship to allow rapid accretion of evidence where it exists:

Management is supported by the NHSE. It already has about 150 articles from ***Bandolier*** and ***ImpAct*** concerning management, evidence, and change.

The Oxford Pain Internet Site was previously sponsored by the BUPA foundation and MSD to get it started, and results of more meta-analyses and other evidence continue to be added.

Complementary therapy is sponsored by the BUPA Foundation. Systematic reviews and other evidence on complementary and alternative therapy are being abstracted and added to the site. Many more will be added this month.

Migraine is being sponsored by the Gwen Bush Foundation and MSD. This has only just started, but rapid growth will be seen in the next few months.

Healthy living is without sponsorship. ***Bandolier*** considers this to be a topic of such importance that the work is being done despite not having resources to do it.

Monthly email alert

We are also experimenting with one further service. If you register your email address with ***Bandolier*** we will email you each month when a new issue goes live. The email will tell you what is new on the Internet site each month. This will also be accessible from the home page.

Enjoy the paper version, but there's more on the Internet.

In this issue

*The views expressed in **Bandolier** are those of the authors, and are not necessarily those of the NHSE*

Everything ever in *Bandolier* and *ImpAct* and much more at www.ebandolier.com

ANTENATAL
CORTICOSTEROID THERAPY

"The first RCT on the effects of giving a short course of corticosteroids to women expecting to give birth prematurely was reported in 1972. The Cochrane Collaboration logo summarises the evidence that would have been revealed had a systematic review of available RCTs been performed a decade later in 1982. Those who have seen the logo will notice a diamond lying to the left of a vertical line which indicates no effect; this marks that the result produced significant benefit when the results of seven trials were combined.

The reality was that it was 1989 that a systematic review of the RCTs had been prepared and published, but the problem seems to be that uptake of knowledge is very slow."

These words appeared in ***Bandolier*** 13 in 1995, but the issue of steroids in preterm delivery had been examined in issues 1 and 2 of ***Bandolier***. There is an historic context as well, because as long ago as 1970 ***Bandolier*** was working on tests of foetal pulmonary maturity. By 1976 they were no longer needed because of the use of steroids. What a surprise, then, in 1993 to sit in meetings discussing the promotion of their use in the same hospital in which their use was standard practice 16 years previously.

Now it's déjà vu all over again as a randomised trial is published testing mechanisms to increase uptake of their use in appropriate women [1]. The study has the merit of giving good advice about how complex organisations can make sure that the right thing is done right more often.

Study

This was a study in which 27 hospitals were randomised to a usual dissemination intervention or an active dissemination intervention. This followed the NIH consensus panel recommendations (***Bandolier*** 13). The hospitals were all tertiary care facilities with neonatal intensive care units, those most likely to adopt the NIH recommendations about the use of preterm steroids faster.

Usual dissemination included mailing a brochure on the NIH recommendations to hospitals, universities, medical societies and obstetricians, and via the American College of Obstetricians and Gynecologists to its membership. The recommendations were also carried in JAMA and a supplement to the American Journal of Obstetrics and Gynecology.

Intervention hospitals, in addition received a staggered five-component series of actions, comprising:

1 An influential physician and nurse coordinator at each hospital to influence institutional dissemination.
2 A grand rounds lecture on the use of preterm steroids by a nationally respected expert.
3 A chart reminder system to prompt physicians to consider prescribing therapy on a timely basis.
4 Group discussions led by influential physicians discussing four case scenarios in which steroids might be used.
5 Monitoring of care by providing feedback to physicians. Nurse coordinators kept logs of admissions and deliveries.

Medical charts from 3516 women were examined in the baseline year (to February 1994), and 3282 in the year following the NIH conference proceedings (April 1995 to July 1996). These were eligible cases including all women giving birth at 34 weeks or less, including cases of spontaneous preterm labour, premature rupture of membranes, and preterm delivery indicated for medical conditions.

Results

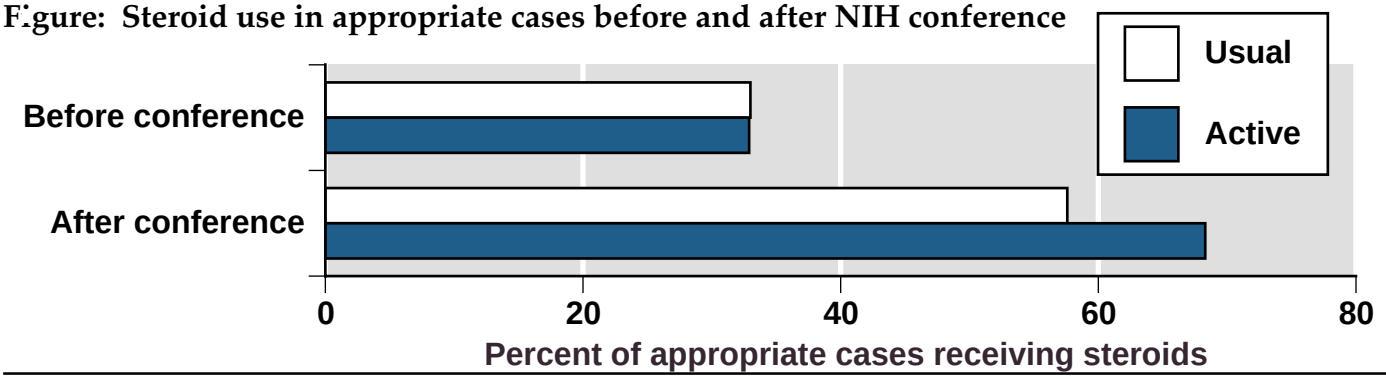
In the year before the NIH conference, steroids were used in 33% of appropriate women. Usual dissemination increased this to 58% of appropriate women in the year after the conference, an increase of 75%. Active dissemination gave a significantly greater increase to 68% of appropriate women, an increase of 105% (Figure).

Comment

At a minimum active dissemination hastened the adoption of steroid therapy by 13 women per hospital in the first year. Given the reduction in morbidity and mortality these results are important. The estimate was that cost savings of $3000 per treated neonate in intensive care resulted from the use of preterm steroids. The estimate for the costs of active implementation were between $77 and $1231 per treated neonate, depending on how costs of active dissemination were determined.

Active dissemination of good evidence benefits patients, and reduces cost burdens on institutions. The paper is worth a read because of the way it describes how active dissemination can be done, generically and not just specifically for this particular condition.

Figure: Steroid use in appropriate cases before and after NIH conference



The paper also discusses considerable inter-hospital variation, both in initial use of steroids and in their uptake. Institutions are complex organisations, and the paths of righteousness are seldom straight. So whatever is attempted needs to take account of local conditions and overcome local problems.

The bottom line, though, is that the paper is one that answers the question about whether adoption of the evidence makes things better. Sure does.

Reference:
1 LC Leviton et al. Methods to encourage the use of antenatal corticosteroid therapy for fetal maturation. A randomized controlled trial. JAMA 1999 281: 46-52.

ZYBAN FOR SMOKING CESSATION

Is this new Zyban stuff really any good for stopping people smoking? That's a recent question put to ***Bandolier*** by several readers. Not an easy one to answer until someone draws your attention to the fact that bupropion (Zyban) has been included in a Cochrane review on the use of anxiolytics and antidepressants for smoking cessation [1].

There are apparently two reasons to believe antidepressants and anxiolytics might help in smoking. First, anxiety and depression are symptoms of nicotine withdrawal, and smoking cessation sometimes precipitates depression. Second, smoking appears to be due, in part, to deficits in dopamine, serotonin and noradrenaline, all of which are increased by anxiolytics and antidepressants.

Search

This involved a typically thorough Cochrane search, using the trial register maintained by the Cochrane Tobacco Addiction Group. Randomised trials compared anxiolytic or antidepressant drugs to placebo or to an alternative therapeutic control for smoking cessation and with at least six months follow-up, and using the most rigorous definition of abstinence.

Results

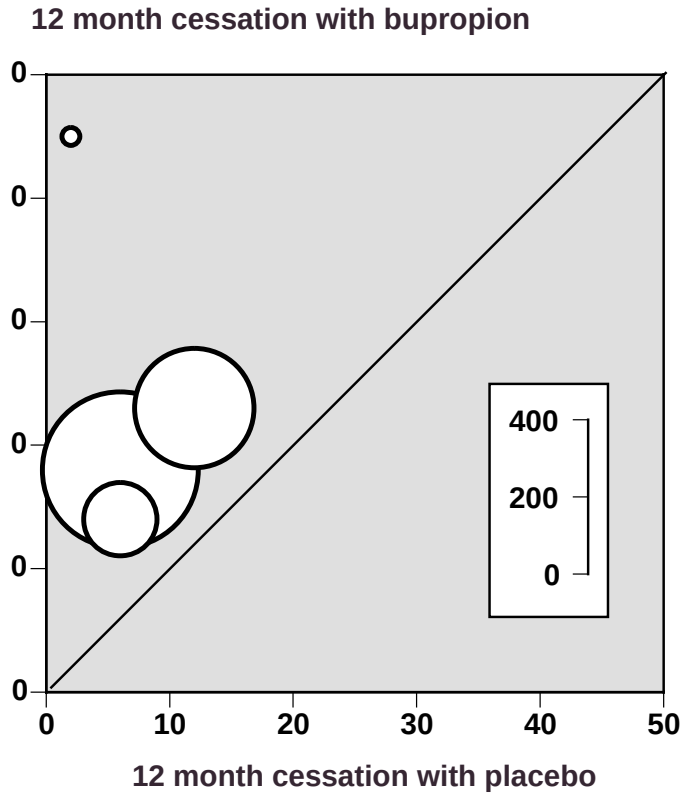
For most anxiolytics and antidepressants there was only a single trial, but two of nortriptyline and four of bupropion. Only these latter two drugs increased smoking cessation.

For bupropion, four randomised studies compared 12-month cessation rates with placebo. For bupropion 300 mg a day for seven to 12 weeks, 105/518 (20%) smokers had stopped at 12 months, compared with 34/430 (8%) with placebo (Figure). The relative benefit was 2.6 (95% confidence interval 1.8 to 3.8) and the number needed to treat was 8.2 (6.1 to 13).

Comment

Bupropion looks better than nicotine replacement therapy. The placebo response rate is the same, but cessation rates

Figure: Smoking cessation at 12 months with bupropion and placebo



are higher, and the NNT, at 8, is lower than that for most nicotine replacement therapies, at about 12-15 (***Bandolier*** 54). Given that the smoking of cigarettes has such major health consequences (***Bandolier*** 9, 14), clearly there will be benefits for some people. Smokers don't have to be depressed to use bupropion. There are adverse effects, and the review [1] quotes a risk of seizures estimated at 1 in 1000, as well as minor adverse effects like nausea and insomnia, but without numbers.

The other comment is just how useful the Cochrane Library is becoming. The latest issue has over 800 reviews, and it will soon top 1000. Quick literature searches elsewhere reveal that the total number of systematic reviews is probably of the order of 5,000 to 10,000, many of which are poor or out of date, so Cochrane is fast coming to house a significant proportion of all worthwhile reviews. The Library also houses many sources of other reviews as well. There may be some way to go to make the Library less clunky and the reviews more user friendly, but that will come.

What we could do with is a single source of all known systematic reviews. This has been done for particular areas, but knowing that there was a single place to search for reviews, good or bad, would be a decided advantage, and not a particularly difficult job.

Reference:
1 JR Hughes, LF Stead, T Lancaster. Anxiolytics and antidepressants for smoking cessation (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2000. Oxford: Update Software.

TREATMENTS FOR INFANT COLIC

Infants who cry for hours, day after day, and for no obvious reason try parents, families and carers. The worry is that something is wrong, but much more often than not the crying is due to infantile colic. It's not uncommon, affecting 1 in 6 to 1 in 4 infants during the first months of life.

A systematic review of treatments with NNTs in the abstract [1] seems like a godsend, especially when some of those NNTs are low. But beware reading abstracts, because behind the abstract we learn how flimsy are the conclusions for those NNTs. A frustration with the evidence-based approach can be that it tells us just how little we know. Defining the research agenda is wonderful for academics, but we have a screaming child and we want the answer NOW! ***Bandolier*** has misgivings about evidence when there's actually precious little of it. But infant colic affects up to 150,000 of the children born in the UK every year, and for such a common condition, on balance, a brief reprise of the evidence available probably makes sense.

Search

The review sought randomised trials of infant colic in English from MEDLINE, the Cochrane Library, books and review articles.

Results

There were 23 comparisons in 22 reports, 12 of which were considered adequately to describe double-blinding, and nine of which adequately defined cases using the Wessel definition of colic. This is unexplained paroxysmal bouts of fussing and crying that lasted more than three hours a day, for more than three days a week, and for more than three weeks. Seven studies examined pharmaceutical interventions, eight dietary interventions, four behavioural interventions and three naturopathic interventions. The trials were small. Three comparisons had fewer than 25 infants, 12 between 26 and 50, five between 51 and 100 and three between 101 and 166.

The results are shown in the Table. While occasional studies demonstrated some effect, most are likely to be subject to bias. Sucrose studies were of reasonable standard, if small, but showed only brief effect. Dicyclomine studies were of variable quality, but potentially severe adverse effects, including apnoea, preclude its use. Hypoallergenic diets for mothers and infants in studies of mixed quality may have small effects, but their reporting is confusing, and confounded by small numbers, as most of these trials.

Comment

There's no more, at least not up to May 1999. Placebo treated groups had improvement in 5% to 83% of infants. Most of this variability could be the random play of chance, on top of any methodological problems, of which there were many. Only five of the 22 studies were randomised, double blind and had adequate case definition. Only two of those, on sucrose, were about treatments we might use.

The simple fact is that there is no evidence that any intervention is effective. For today's mums and dads all we can offer is the knowledge that their screaming infant will grow out of it.

Reference:

1 MM Garrison, DA Christakis. Early childhood: colic, child development, and poisoning prevention. A systematic review of treatments for infant colic. Pediatrics 2000 106: 184-190.

Table: Trials of interventions for infant colic

Treatment	Number of trials	Number of infants	Comment
Simethicone	3	272	Three trials with adequate double blinding showed no evidence for efficacy
Dicyclomine	3	134	Dicyclomine better than placebo in three trials, one adequately double blind. Adverse effects, some serious reported in infants and drug contraindicated in infants less than 6 months
Soy formula	2	158	One study showed good improvement, while larger of the two did not permit analysis.
Increased carrying	2	94	No effect
Hypoallergenic formula	2	72	Some indication that hypoallergenic formula has a beneficial effect in two studies
Sucrose	2	72	Sucrose appears to be effective only for a short while
Lactase enzymes	2	44	No difference between lactase enzymes and placebo
Hypoallergenic diet	1	115	Complicated because breast feeding mothers and bottle-fed infants included in trial. May be a small reduction of daily colic symptoms of 25%, but complicated design and inconsitant result reporting
Herbal tea	1	68	May be slight effect in single study, but sensible parents unlikely to try this in small infants
Fibre enriched formula	1	54	No effect
Decreased stimulation	1	42	Bare significance in trial with potential for much bias
Methylscopolamine	1	40	No benefit of treatment and more adverse effects
Dairy elimination diet	1	40	No benefit of treatment
Car ride simulator	1	32	No effect
Parent training	1	14	No effect in tiny flawed trial

TREATMENTS FOR IRRITABLE BOWEL SYNDROME

Irritable bowel syndrome (IBS) is said to affect about 1 in 5 women and 1 in 10 men, and be a major reason for visits to GPs and gastroenterologists. For all this, there is a surprising lack of effective treatments, and textbooks are often surprisingly unhelpful. A new systematic review [1] may not provide all the answers, but it turns an impenetrable fog into a heavy mist, and gives some clues for patients and their carers.

Search and inclusions

Comprehensive searching of four databases, including the Cochrane Library was supplemented by manual searches of bibliographies, but only for English language reports. For inclusions a trial had to satisfy six criteria:

- Treat irritable bowel syndrome.
- Study adult patients.
- Administer a pharmacological intervention to more than 10 patients for at least two weeks.
- Include a placebo control group.
- Report outcome measures of global improvement or individual symptoms or both.
- Be randomised and double blind.

A qualitative assessment of the validity of trials was done, and high quality studies were assessed separately.

Results

There were 70 studies found, of which 28 were judged to be of high quality / validity. It was not possible to combine information, and vote counting was used. For the high quality studies the results are shown in the Table.

Only three interventions had a high proportion of positive trials (minimum of two studies and100 patients). Smooth muscle relaxants were consistently effective in reducing abdominal pain associated with IBS, with NNTs for individual trials in the range of 2 to 6. Loperamide was effective in treating diarrhoea associated with IBS. 5HT receptor antagonists appeared to be effective both in terms of global improvement and some individual symptoms, though at the cost of a degree of constipation perhaps.

Comment

There does seem precious little to say about effective treatments for such a common and often distressing condition. But there are some clear indications about what doesn't work or where there is no evidence. Rumours abound about new treatments for IBS making their appearance in the next few years, and at least we know where we start from. The paper also comments on length of follow-up for high-quality trials - twelve weeks. It is interesting that there was only a single small trial for amitriptyline, and that other favoured treatments were supported by no high-quality trials. Make one think.

Reference:
1 J Jailwala, TF Imperiale, K Kroenke. Pharmacologic treatment of the irritable bowel syndrome: a systematic review of randomized, controlled trials. Annals of Internal Medicine 2000 13: 136-147.

Table: High quality trials in IBS

Treatment	High quality trials (positive/total)	Number of patients	Comment
Bulking agents	3/7	341	Possible positive effects from ispaghula husk, but only one of the three positive studies was of sensible size
Smooth muscle relaxants	7/7	701	Consistent improvement in abdominal pain, with NNTs reported from individual trials between 1.6 and 6.7, but no overall value because five different drugs studied. Including lower quality studies, 13 of 16 were beneficial.
Prokinetic agents	1/4	266	No evidence of any benefit
Loperamide	2/2	100	Both studies had improvement in diarrhoea, including frequency of bowel movements, but not abdominal pain or distention
5HT receptor antagonists	2/2	420	Both studies showed global improvements and improvements for some symptoms. Constipation a common adverse effect in one large study of alosetron
Chinese herbal medicine	1/1	116	Global improvement
Peppermint oil	1/1	110	Improvement in symptoms of abdominal pain, distention, stool frequency
Amitriptyline	1/1	14	Trivial data

More on NSAID adverse effects

But definitely the last word for a while. ***Bandolier*** has been pressed by readers to reprise this topic, and to include more than just the gastrointestinal adverse effects. Coincidentally there are several important studies just published that make this possible. A common motif is that adverse effects are problematical in the elderly.

Gastrointestinal AEs

Epidemiological studies associating NSAID use and upper GI problems and published in the 1990s have been reviewed and the data pooled [1] to give a much clearer picture of risks. To be included studies had to:

- Be case control or cohort studies on non-aspirin NSAIDs
- Include data on bleeding, perforation, or other serious upper gastrointestinal tract event resulting in hospital admission or referral to a specialist
- Have data to calculate relative risk

Results

Eighteen studies were found. All had specific definitions of exposure and outcome and similar ascertainment for comparison groups. All but two attempted to control for potential confounding factors, like age, sex, history of ulcer or concomitant medicines.

The main results are summarised in Figures 1 and 2. Compared with nonusers, NSAID users had a higher risk of upper GI bleed (UGIB) when they were current NSAID users and used a higher dose. The duration of use was unimportant, but different NSAIDs had different risks, with ibuprofen (especially doses below 2400 mg a day) being least harmful.

The effect of ulcer history and age is shown in Figures 3 and 4. People with a history of ulcer or with a previous bleed who took NSAIDs were at much greater risk than those with no history of ulcer who took NSAIDs. Older folk who took NSAIDs were at greater risk than under 50s who took NSAIDs.

Figure 1: Risk of UGIB for NSAID users compared with nonusers

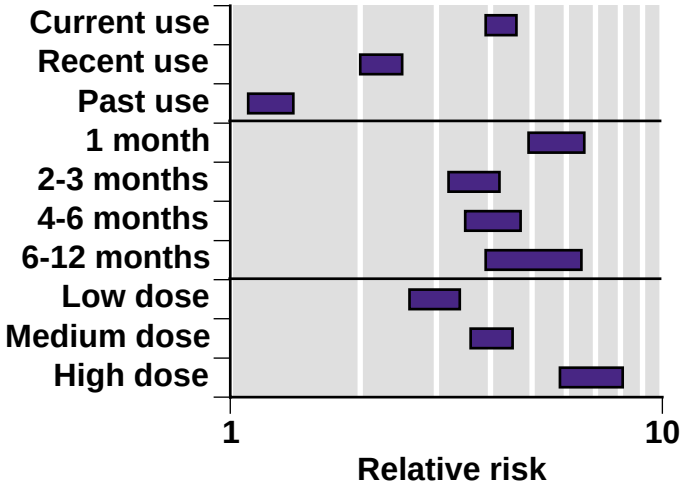


Figure 2: Risk of UGIB for particular NSAIDs, users compared with nonusers

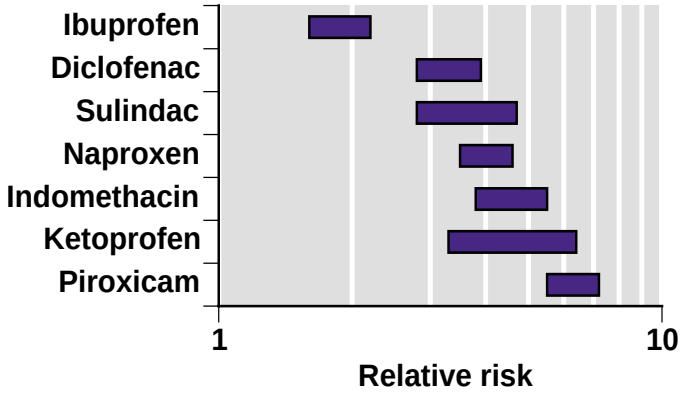


Figure 3: Effect of history of ulcer in users of NSAIDs

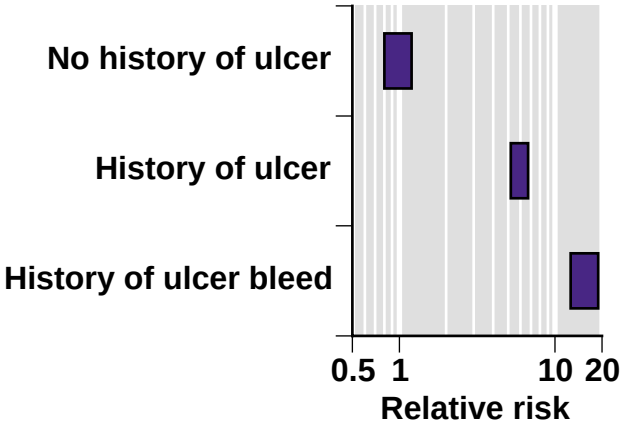
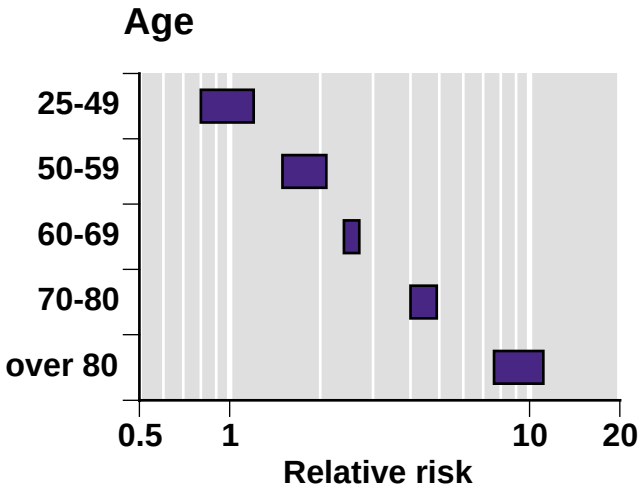


Figure 4: Effect of age in users of NSAIDs

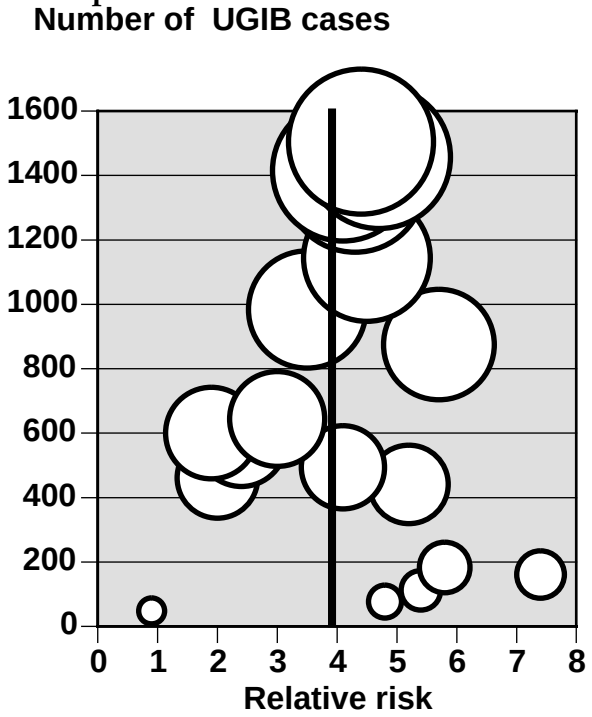


In this set of high quality studies, there was a clear effect of size on the estimate of relative risk of upper gastrointestinal bleed with NSAID. The pooled estimate was 3.8 (3.6 to 4.1). With fewer than 1000 cases, the results of individual studies was highly variable (Figure 5).

Renal failure

People who work in renal units will tell you about the association between NSAIDs and acute renal failure. The problem has been to get a reliable estimate of the risk. There have been some small studies, but a new, large study from Tennessee gives us a better picture [1].

Figure 5: Effect of size of study in determining overall relative risk of GI bleed, NSAID users compared with nonusers



The study was conducted among all members of the Tennessee Medicaid programme aged 65 years or more in 1987-1991 and enrolled for at least one year. Those with first admission to hospital for acute renal failure (admission creatinine level of 180 μmol/L or more at admission) were the cases of community acquired acute renal failure. Controls were randomly selected for all persons in the study population. Exclusions were people with end stage renal disease and those with hospital acquired acute renal failure. NSAID exposure was ascertained from prescriptions filled in the year before the index date.

Results

There were 1,799 cases with an annual incidence of community acquired acute renal failure of 4.5 admissions per 1000. The median hospital stay was eight days. Thirty-six percent died within 30 days. Forty-two percent were classified as having new renal disease. The remainder were classified as having chronic renal failure with acute exacerbation based on a prior creatinine level above 122 μmol/L, a documented history of chronic renal failure or imaging studies compatible with chronic renal disease. There were 9,899 controls. Controls were less likely to be nursing home residents or be 85 years or older.

NSAID use was higher (18%) in cases than in controls (11%). For current NSAID use the odds ratio was 1.6 (95% confidence interval 1.3 to 1.9). Those who had stopped using NSAIDs within the past 30 days had no increased risk of renal failure. For certain NSAIDs where there was sufficient information, ibuprofen and indomethacin, there was a dose response for risk. For individual NSAIDs, ibuprofen, piroxicam, fenoprofen and indomethacin had the greatest increased risk, with odds ratios of about 2.

A previous detailed study [3], though on smaller numbers, indicated that previous renal disease, or gout, but particularly a joint history of gout plus previous renal disease were major risks for renal failure with NSAIDs. Patients using NSAIDs with half lives of 12 hours or more in the previous week had particularly increased risk of renal failure.

Congestive heart failure

It seems as if we also have to begin to worry about NSAIDs being related to congestive heart failure (CHF) in older people [4].

This study at two hospitals in New South Wales (population about 450,000) enrolled as cases consecutive patients between 1993 and 1995 where the medical officer admitting the case and the attending physician agreed that the primary reason for admission was CHF. Patients admitted for other reasons with incidental CHF were not included. Study nurses ensured that all included cases met Framingham criteria for CHF. Controls (target two per case) were patients of the same sex and within five years of age admitted to the same hospital, but with no clinical or radiological signs of CHF.

Results

There were 365 cases and 658 controls, with a mean age of 76 years. Most cases had moderate or severe CHF. Use of nonaspirin NSAIDs was 17% in the cases in the week before admission, compared with 12% in controls. The adjusted odds ratio was 2.1 (5% confidence interval 1.2 to 3.3) for all cases, and 2.8 (1.5 to 5.1) for the 272 cases with first admission for CHF (Table 1).

CHF was far more likely in those patients with a prior history of heart disease, in which the odds ratio was 26 (5.8 to 119). Complicated statistical analysis confirmed the effect of pre-existing heart disease, and suggested that NSAIDs with longer half lives (naproxen, piroxicam, and tenoxicam) had much higher risk than those with short half lives (ibuprofen, diclofenac, for instance), though on small numbers in a subgroup analysis.

Comment

Table 2 puts all this into the perspective of an average PCG of 100,000 [5] for the over '65s. In this group there would be 18 hospital admissions every year for upper gastrointestinal bleeding, 10 for acute renal failure and 22 for congestive heart failure. These latter seem high, but in both cases the bulk of the events would be in those aged 75 and over. Age is certainly the issue.

Table 1: NSAID use and history of heart disease on risk of developing CHF

Heart disease	NSAID use	Odds ratio (95% CI)
No history	Nonuser	1
No history	User	1.6 (0.7 to3.7)
History	Nonuser	2.5 (1.4 to 4.3)
History	User	26 (6 to 119)

Table 2: NSAID adverse effects in an older population of an average PCG

Event	Cases per year
Upper GI bleed	18
Acute renal failure	10
Congestive heart failure	22

Information based on an average PCG of 100,000 patients where 3,800 over '65s take NSAIDs

For both renal failure and CHF NSAIDs seems to uncover incipient disease. For renal failure there are several, smaller, confirmatory studies, and for CHF at least one [6]. For both there appears to be a plausible mechanism, dose-response relationships, and particular association with NSAIDs with longer half lives. Renal failure has a high mortality, and CHF is also serious, as treatment is unlikely to restore patient's functioning to previous levels.

The good news is that for most older patients sensible assessment and pertinent guidance should mean that many of these events could be avoided. While the new coxibs are not associated with elevated risks of gastrointestinal bleeding, there is no evidence, or indeed likelihood, that they will not precipitate renal failure or CHF.

Put in a humanitarian and economic context, these 50 first hospital admissions a year (Table 2) per PCG of 100,000 population is equivalent to 30,000 admissions a year in the UK. Most are avoidable. Information we have suggests an average stay of about a week, costing about £1,400 each. That's something like £40 to £50 million a year for the NHS.

Reference:

1 S Hernández-Diaz, LA García Rodriguez. Association between nonsteroidal anti-inflammatory drugs and upper gastrointestinal tract bleeding and perforation: An overview of epidemiological studies published in the 1990s. Archives of Internal Medicine 2000 160: 2093-2099.

2 MR Griffin, A Yared, WA Ray. Nonsteroidal antiinflamatory drugs and acute renal failure in elderly persons. American Journal of Epidemiology 2000 151:488-496.

3 D Henry et al. Consumption of non-steroidal anti-inflammatory drugs and the development of functional renal impairment in elderly subjects. Results of a case-control study. British Journal of Clinical Pharmacology 1997 44: 85-90.

4 J Page, D Henry. Consumption of NSAIDs and the development of congestive heart failure in elderly patients: An underrecognized public health problem. Archives of Internal Medicine 2000 160:777-784.

5 AL Blower, A Brooks, CG Fenn et al. Emergency admissions for upper gastrointestinal disease and their relation to NSAID use. Aliment Pharmacol Ther 1997 11: 283-91.

6 ER Heerdink et al. NSAIDs associated with increased risk of congestive heart failure in elderly patients taking diuretics. Archives of Internal Medicine 1998 158:1108-1112.

TUBERCULOSIS DIAGNOSIS

A study showing how diagnostic test evaluation should be done [1] integrated a new genetic test for tuberculosis with clinical suspicion versus the gold standard. Consecutive patients suspected of TB were classed as low (less than 25%), intermediate (26% to 75%) or high risk (more than 75%) based on standard workup including history, clinical examination and risk factors. The Enhanced Mycobacterium tuberculosis Direct (E-MTD) test was done but not reported.

Fortunately data used for calculating the sensitivity and specificity were available, because likelihood ratios were not given. ***Bandolier*** guessed that probability of having TB of over 50% might well result in antimicrobial therapy. All high risk patients would have been treated anyway, but a positive E-MTD test in low and intermediate risk groups would also result in treatment. The AFB test was unhelpful. ***Bandolier*** guessed that only when the post-test probability of having TB was below 1% might the diagnosis be dismissed. A negative E-MTD test did this for the low, but not intermediate or high risk groups. The AFB test was useless for ruling out the diagnosis.

Reference:

1 A Catanzaro et al. The role of clinical suspicion in evaluating a new diagnostic test for active tuberculosis. Results of a multicentre prospective trial. JAMA 2000 283: 639-45.

Complete abstract on ***Bandolier*** website

Clinical suspicion	TB (%)	Positive likelihood ratio	Negative likelihood ratio
E-MTD			
Low	5	**25.2**	**0.17**
Medium	29	**72.0**	0.25
High	87	**10.5**	0.15
Overall	21	**31.7**	0.17
AFB			
Low	5	**17.7**	0.6
Medium	29	1.1	1.0
High	87	**2.5**	0.3
Overall	21	7.2	0.44

Shaded block: indicates a rule-in decision for post-test probability of 50% or greater for positive likelihood ratio. A negative likelihood ratio indicates a rule-out decision where post-test probability less than 1%.

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